

### REMARKS

Claims 5-10 stand rejected under 35 U.S.C. 103(a) as being unpatentable over U.S. Patent 5,478,812 to Murase et al ("Murase") in view of Cynshi et al, PNAS, (1998) ("Cynshi"). The Office Action, coupled with previous Office Actions, asserts that Murase teaches that chromanol glucoside in vitro is an antioxidant and that Cynshi teaches that antioxidants can be useful in treating arteriosclerosis, therefore rendering the instant claims obvious. This rejection is respectfully traversed.

To establish a *prima facie* case of obviousness, the Patent and Trademark Office must demonstrate by substantial evidence that the prior art relied upon, coupled with the knowledge generally available in the art at the time of the invention, contains some suggestion or incentive that would have motivated an ordinary skilled person to modify the subject matter of a reference or combine the subject matter of the references to achieve the claimed subject matter. *In re Fine*, 837 F.2d 1071, 1074 (Fed. Cir. 1988). Furthermore, "the mere fact that references can be combined or modified does not render the resultant combination obvious unless the prior art also suggests the desirability of the combination." *In re Mills*, 916 f.2d 680 (Fed. Cir. 1990).

In the instant case, Cynshi does not assert that all anti-oxidants are, or even potentially are, arteriosclerosis treatments. Cynshi reports the results of a study for one novel anti-oxidant compound (BO-653) specifically designed for the study. The article discloses the known drawbacks for two anti-oxidant compounds (probucol and  $\alpha$ -tocopherol) and then compares the performance of BO-653 to those known compounds. No further assertion or teaching relative to other specific anti-oxidants, or ant-oxidants in general, are made in Cynshi.

In fact, Cynshi could easily be read by one of ordinary skill in the art for the general suggestion that relatively few anti-oxidants can be used as an effective arteriosclerosis treatment. Cynshi discloses that 600 newly synthesized anti-oxidants were screened with the most promising compound having only mixed results as an arteriosclerosis treatment. Further, Cynshi actually highlights the deficiency of two well known anti-oxidants as therapeutic agents, including  $\alpha$ -tocopherol, which as a result tends to teach away from the present invention.

Cynshi states that  $\alpha$ -tocopherol, which is a liposoluble anti-oxidant, is reported as having only modest effect to no effect on spontaneous development of arteriosclerosis. See page 10123. It also states that  $\alpha$ -tocopherol cannot exert its antioxidative effects on the core of LDL. Yet the present invention discloses a derivative of  $\alpha$ -tocopherol. So to the extent that Cynshi identifies a problem with known anti-oxidants, it does not teach or suggest combining the teaching of Murase as the solution. The structure of BO-653 is significantly different from that of the present invention and is different from  $\alpha$ -tocopherol. It certainly does not suggest that the solution to the problem is in the form of an  $\alpha$ -tocopherol derivative like the present invention.

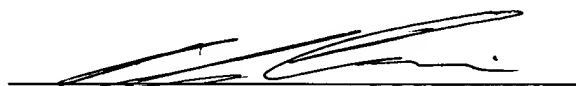
This difference in structure is of critical importance as it relates to the solubilities of Cynshi compounds (BO-653, probucol and  $\alpha$ -tocopherol) compared to the presently claimed compounds. The Cynshi compounds, including BO-653 are lipophilic while chromanol glucoside is water soluble. This difference, coupled with the notion that Cynshi emphasizes the drawbacks of  $\alpha$ -tocopherol, do not provide any motivation for one of ordinary skill in the art to combine Cynshi with Murase to form the invention as presently claimed.

With regard to Murase, the object of the invention, "is to provide a chromanol glycoside, a novel water-soluble antioxidant excellent in chemical stability and usable as a solution making use of the chroman ring of outstanding antioxidant activity, and a method for the production of the chromanol glycoside." See Column 1, lines 62-67. To the extent that Murase meets this objective, it does not provide any teaching with respect to the treatment of arteriosclerosis. Arteriosclerosis is singularly mentioned in the background as a condition, among other conditions including cancer and aging, that may have some connection to the formation of lipid peroxide, but the reference does not suggest that chromanol glycoside could treat these conditions.

In view of the foregoing, Applicants submit that all pending claims are in condition for allowance and request that all claims be allowed. The Examiner is invited to contact the undersigned should he believe that this would expedite prosecution of this application. A request for an extension of two months accompanies this response along with a check for the fee. It is believed that no fee is required. The Commissioner is authorized to charge any deficiency or credit any overpayment to Deposit Account No. 13-2165.

Respectfully submitted,

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